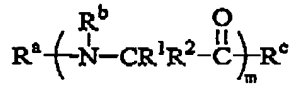
REMARKS

Claims 13-17, 21, 24-29, and 33-35 are now pending. Claims 13-17, 21, 24-29 have been examined. Claims 13-17, 21, 24-29 have been rejected. Claims 33-37 have been added in the present amendment.

Independent claim 13 has been amended to recite "providing a library of peptoids having a plurality of unknown sequences" and "contacting a plurality of unknown peptoids in the library with an oligonucleotide". Support for this amendment can be found on page 8, fourth paragraph; page 15, third paragraph; and in Figure 2. Independent claim 13 has also been amended to include all of the limitations of claim 24 and an additional limitation on formula I where "at least one of R^a and R^c comprises a lipid moiety".



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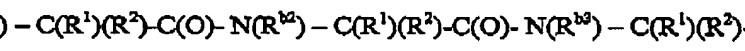
Support for this amendment can be found on page 12, second and third paragraphs, page 14, second paragraph; in Figures 1C, 1D, and 3; and in claim 24.

Claim 15 has been amended to recite, "said peptoids are supported on solid particles in said physically separated compartments". It is supported in the specification at page 17, last paragraph.

A new claim 33 has been added. It recites "The method of claim 13, wherein said terminal peptoids having a plurality of unknown sequences have the general formula II:



II

where

R^{b1} is a non-cationic moiety, R^{b2} is a non-cationic moiety, R^{b3} is a cationic moiety; and

n is an integer selected from 2 to about 16."

It is supported by Figures 1C, 1D, and 3; and by claim 24.

A new claim 34 reciting, "The method of claim 13, wherein said peptoids comprise at least two different cationic moieties" is supported in the specification at page 17, second paragraph and in Figure 3.

A new claim 35 reciting, "The method of claim 13, wherein said library is synthesized by a mix-and-split protocol" is supported in the specification at page 17, third paragraph; and page 23, last paragraph.

A new claim 36 reciting, "The method of claim 13, wherein identifying transfecting peptoids comprises determining their sequence" and its dependent claim 37 reciting, "The method of claim 36, wherein the peptoid sequence is determined by a mass spectrographic method " are supported in the specification at page 19, last paragraph, and at page 20.

Other claims have been amended to make minor clerical changes.

All rejected claims were rejected based on US Patent No. 6,153,596 issued to Liotta et al., a PNAS publication by Murphy et al., and US Patent No. 6,677,445 B1 issued to Innis et al.

As explained below, the pending claims are respectfully submitted to be patentable over these references. Of particular note, both Murphy and Liotta teach transfection of cells with peptoids of *known* sequence.

Rejections based on 35 USC 112 first paragraph

Claims 13-17, 21, and 24-29 were rejected under 35 USC 112 first paragraph for inadequate written description. The Office Action suggested that incorporation of the structure of claim 24 to claim 13 would obviate this rejection. The Applicants appreciate this suggestion and have amended claim 13 to include the structure of claim 24. Withdrawal of the written description rejections is therefore respectfully requested.

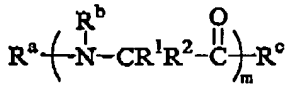
Rejections based on 35 USC 112 second paragraph.

Claim 16 was rejected for the lack of antecedent basis in claim 15 for the "particles in said compartments" language. The Applicants appreciate that this deficiency was noted by the Examiner and it has been corrected by amending claim 15 to recite "solid particles in said physically separated compartments."

Claim 24 has been rejected as confusing in the recitation of the clause "wherein at least one group R^b is not hydrogen".

The Applicants note that formula I of claim 24 depicts an oligomer in which the unit

$-N(R^b) - C(R^1)(R^2)-C(O)-$ is repeated m times. The substituents R^b, R^1 and R^2 need not be the same throughout the oligomer. In fact, variations of these substituents in one oligomeric molecule present an important embodiment of the invention.



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It should be understood that an oligomer of general formula I may have up to m different substituents R^b. The Applicants believe that claim 24 clearly suggests that R^b may be different within one oligomeric species, and that it is especially clear in light of specification, for example the species described at page 16, last paragraph, and Figure 3. The Applicants, therefore, respectfully submit that the claim is not ambiguous in its present form, and withdrawal of 112 second paragraph rejections for claims 16 and 24 is respectfully requested.

Double Patenting Rejections based on Innis et al.

The Office Action cites US Patent No. 6,677,445 B1 issued to Innis et al. as the basis for a nonstatutory double patenting rejection of claims 13-17, 21, and 24-29. Specifically, the Office mentions claims 1-2 of the Innis patent and also refers to the Innis patent's written description. In claims 1 and 2 of the Innis patent the *compositions* of oligonucleotides and terminal lipitoids are claimed. It is respectfully submitted that the claims to these compositions do not render obvious the claim to a "*method* of identifying peptoids". The Applicants also point out that it is not appropriate to rely on written description of a patent for an obviousness-type double patenting rejection. Only inventions *as claimed* can be evaluated, with the written description serving merely as a dictionary for claim interpretation.

"Any obviousness-type double patenting rejection should make clear:

(A) The differences between the inventions defined by the conflicting claims – a claim in the patent compared to a claim in the application; and

(B) The reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent.

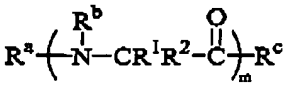
When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art" (MPEP, section 804).

The *claimed* invention of the Innis patent does not render obvious the invention defined in the claims of the present application. The Applicants, therefore, respectfully request withdrawal of the double patenting rejection for claims 13-17, 21, and 24-29.

Rejections based on 35 USC 102(e)

Claims 13 and 21 have been rejected by the Office as anticipated by Liotta et al. (USP 6,153,596). The Applicants have amended the independent claim 13 to clarify the distinction between the method of claim 13 and the method used by Liotta. Claim 13 as amended recites: "A method of identifying peptoids which are effective in transfecting a cell with an oligonucleotide, the method comprising

(i) providing a library of peptoids having a plurality of unknown sequences and having the general formula I:



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where R^a is selected from the group consisting of alkyl, aryl, aralkyl, aralkenyl, and aralkynyl, any of which may be substituted with one or more groups X; hydrogen, -OH, -SH, -COOH, sulfonyl, and a lipid moiety, wherein said lipid moiety may be conjugated to a linker moiety,

each R^b is independently selected from the group consisting of alkyl, aryl, aralkyl, aralkenyl, and aralkynyl, any of which may be substituted with one or more groups X; and hydrogen,

wherein at least one group R^b is not hydrogen;

R^c is selected from the group consisting of alkyl, aryl, aralkyl, aralkenyl, and aralkynyl, any of which may be substituted one or more groups X; hydrogen, -OH, -SH, $-NH_2$, -NHR, -NH(C=O)R, where R is lower alkyl; sulfonyl, hydrazine, and a lipid moiety, wherein said lipid moiety may be conjugated to a linker moiety;

X is selected from hydroxy, alkoxy, amino, guanidino, amidino, alkylamino, alkylthio, halogen, nitro, cyano, keto, aldehyde, carboxylic acid, carboxylic ester, carboxylic amide, sulfonic acid and sulfonic ester;

at least one of R^a and R^c comprises a lipid moiety;

R^1 and R^2 are independently selected from hydrogen, lower alkyl, and lower alkoxy; and

m is an integer selected from 2 to about 50.

(ii) contacting a plurality of unknown peptoids in the library with an oligonucleotide, to form a plurality of peptoid-oligonucleotide mixtures, wherein said oligonucleotide is between about 10 and 50 nucleotides in length;

(iii) contacting each said mixture with a cell;

(iv) screening each cell for transfection of the oligonucleotide, to identify transfected cells; and

(v) identifying transfecting peptoids in mixtures contacted with transfected cells."

Liotta et al. does not teach the limitation of "providing a library of peptoids having a plurality of *unknown* sequences" and "contacting a plurality of *unknown* peptoids in the library with an oligonucleotide". Liotta's patent describes transfection method with peptoids of *defined* sequence. Liotta also states that the *known* peptoids are matched by their size and charge to the oligonucleotides to be transfected (column 7, lines 53-67).

Further, as noted in the Office Action, Liotta does not disclose a peptoid of general formula I of claim 24. Formula I is now incorporated into base claim 13. Therefore the Applicants believe that claim 13 as amended is not anticipated by the Liotta patent.

Accordingly, the Applicants respectfully request withdrawal of 102(e) rejections for claim 13 and for its dependent claim 21.

Rejections based on 35 USC 103(a)

The Office Action rejected claims 13-17, 21 and 24-29 under 35 USC 103(a) as being unpatentable over Liotta (USP 6,153,596) in view of Murphy (PNAS). However, the Applicants submit that these claims, as amended, are not rendered obvious to one skilled in the art by a combination of Liotta and Murphy references.

Both Liotta and Murphy are using peptoids of *known* sequence for cell transfection. The Applicants, on the contrary, provide a plurality of peptoids of *unknown* sequence, screen for cell transfection, and only upon successful transfection determine the chemical identity of the transfecting peptoid. The importance of this unobvious distinction will be immediately appreciated by one skilled in the art of drug discovery.

It should be noted that the Applicants' invention as described in the specification is directed towards a transfecting agent discovery method. As a discovery method it is substantially different from the methods of Liotta and Murphy. It is well understood in the art that a drug discovery process may rely on rational design, a combinatorial library approach, or some combination of the two. This equally applies to a transfection agent discovery process. A discovery process usually involves two distinct components – lead generation and lead

optimization. For lead generation, very few rational considerations exist and the library should comprise as many compounds as possible. Lead optimization, on the other hand, has a stronger rational design emphasis, and the library need not be as expansive as in the case for lead generation. Distinct classes of combinatorial libraries, relying on distinct synthetic methods are used in each case.

In rational design methods, some hypothesis is driving the synthesis of defined structures with particular structural properties. The resulting molecules are then tested for activity. For instance, Liotta's hypothesis is that effective transfecting peptoids should have similar size to oligonucleotides, and that they should be able to neutralize or substantially neutralize the oligonucleotide to be transfected. Based on this hypothesis, he proposes to synthesize a library of peptoids with defined size, charge, and structure. In fact, it is critical to know the chemical identity of the peptoid *before* transfection in order to practice Liotta's invention. The library described in Liotta's reference is a rationally designed library of known peptoids. The library described in Murphy is also a library of known-sequence peptoids albeit with a less pronounced emphasis on rational design. It is well known in the art, that libraries of known compounds can be synthesized by parallel synthesis. Parallel synthesis is known to be a rather inefficient combinatorial approach, leading to no more than several hundred compounds in a library. These libraries are suited for lead optimization purposes, but they are not useful for *discovering* leads and identifying *non-designed* effects.

For such a purpose a more expansive library is needed which could comprise thousands or millions of different sequence peptoids, for example. This type of library can be obtained by combinatorial methods other than parallel synthesis, which are not disclosed in the Liotta or Murphy references. As described in the Applicants' specification, this type of library can be synthesized by, for example, a mix-and-split protocol. A mix-and-split approach may lead to millions of combinatorially synthesized peptoids of different and *unknown* sequences. The sequences of peptoids are unknown because the beads containing individual peptoids are mixed during the synthetic procedure. This protocol is superior to parallel synthesis in its efficiency of generating multiple compounds. Such a library of unknown peptoids is well suited for identification of undesigned effects, e.g., for transfection of a cell type that has not been successfully transfected before. This type of library is not described in Liotta's and Murphy's references and cannot be attained by their synthetic procedures.

For at least these reasons, the Applicants respectfully submit that the method claimed in claim 13 is not an obvious variation of Liotta's and Murphy's methods, and withdrawal of the

103(a) rejection for claim 13 and its dependent claims 14-17, 21 and 24-29 is respectfully requested.

CONCLUSION

Applicants believe that all pending claims are allowable in their present form. Please feel free to contact the undersigned at the number provided below if there are any questions, concerns, or remaining issues.

Respectfully submitted,
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